(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
24 June 2004 (24.06.2004)

PCT

(10) International Publication Number
WO 2004/052254 A1

(51) International Patent Classification[7]: A61F 9/013

(21) International Application Number: PCT/EP2003/013955

(22) International Filing Date: 9 December 2003 (09.12.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/432,305 10 December 2002 (10.12.2002) US

(71) Applicant *(for all designated States except AT, US)*: **NOVARTIS AG** [CH/CH]; Lichtstrasse 35, CH-4056 Basel (CH).

(71) Applicant *(for AT only)*: **NOVARTIS PHARMA GMBH** [AT/AT]; Brunner Strasse 59, A-1230 Vienna (AT).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **LISK, James, Reid, Jr.** [US/US]; 3264 Natures Walk, Suwanee, GA 30024 (US). **TAI, Ming-Kok** [MY/US]; 999 Cavesson Terrace, Lawrenceville, GA 30045 (US). **HAMPTON, Scott** [US/US]; 2065 Bethany Spring Trace, Cumming, GA 30041 (US).

(74) Agent: **GRUBB, Philip**; Novartis AG, Corporate Intellectual Property, CH-4002 Basel (CH).

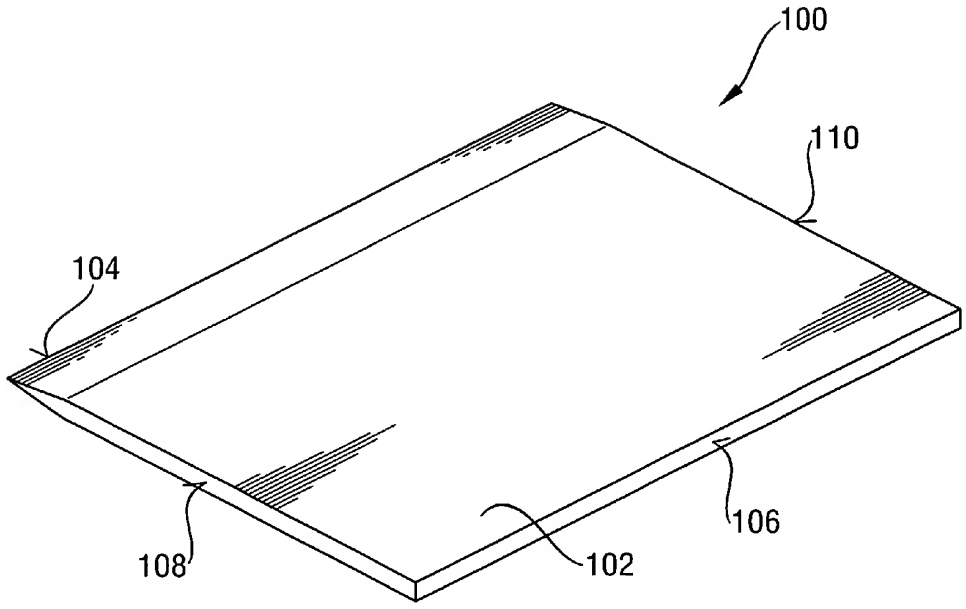
(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SY, TJ, TM, TN, TR, TT, UA, UG, US, UZ, VC, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR).

Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

[Continued on next page]

(54) Title: DISPOSABLE SEPARATOR FOR SEPARATING THE EPITHELIUM LAYER FROM THE CORNEA OF AN EYE



(57) Abstract: A separator constructed of a polymeric material is used with a surgical device that separates the epithelium of a cornea from the underlying Bowman's layer of an eye of a patient. The surgical device includes a positioning ring for temporary attachment to the eye and is structured to present and expose the cornea to be separated. The separator support is structured and disposed to carry the separator. A drive is operably connected to the separator support for causing movement of the separator across the positioning ring and for causing oscillating movement of said separator.

WO 2004/052254 A1

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

Disposable separator for separating the epithelium layer from the cornea of an eye

This invention relates to a blade, in particular to a disposable separator for separating the epithelium layer of a cornea from the underlying Bowman's layer.

BACKGROUND

Microkeratome blades are widely used in LASIK (Laser-Assisted In Situ Keratomilousis) procedures. LASIK permanently changes the shape of the cornea, the clear covering of the front of the eye, using an excimer laser. The microkeratome is used to cut a corneal flap containing the epithelium, Bowman's layer, and a portion of the stroma by slicing through the stroma, dividing it into at least two distinct portions. A hinge of uncut corneal tissue is typically left at one end of this flap. The flap is folded back revealing the penetrated stroma, the middle section of the cornea. Pulses from a computer-controlled laser vaporize a portion of the stroma and the flap is replaced. It is important that the blade used during the LASIK procedure is sharp, otherwise the quality of the procedure and the healing time are poor. Additionally, the blade has to be exceedingly sharp in order to produce consistent and reproducible flaps.

While all currently available microkeratome blades are either stainless or low-carbon steel, a variety of other materials, including diamond, sapphire, tungsten, ceramic, and silicon carbide, have been proposed. Among the known materials, diamond has the best cutting capacity due to its great hardness because the cutting edge can be ground with a very small radius of curvature lying in the nanometer range. Disadvantages are, however, the high material cost and the difficulties in applying the diamond as cutting edge on a knife.

A blade made of stainless steel, on the other hand, can be manufactured in a comparatively simple way, and offers considerable cost advantages. However, while stainless steel blades are cheaper to manufacture than diamond blades, they are not so inexpensive as to render them "disposable" in all instances. Stainless steel blades are sometimes autoclaved after a use and reused on another patient. While autoclaving is generally considered an effective method of sterilization, it is not foolproof, and only one-time use of blades can ensure that each blade is entirely free of infection or physical defects.

Because the "sharpness" of the blade, up until now, has been considered to be the most important characteristic of the blade for achieving a consistent corneal resection, materials cheaper than stainless steel, such as plastics, have been rejected as being too soft to achieve the required sharpness. Instead, the art has focused on various methods of manufacturing ever-more sharp steel blades, resulting in more complex and expensive manufacturing processes.

For instance, both EP 0 119 714 and WO 86/02868 propose to melt the cutting edge of a metallic blade body by laser beam treatment and to rapidly cool it off in a water bath. In this way, the cutting edge is amorphized and can then be sharpened to a radius of curvature less than several ten nanometers.

US Published Application US 2002/0052614 purports to achieve even sharper blades than the above by providing a blade having a carrier portion and a thin-walled cover portion made of amorphous metal, which is joined to the carrier portion. The amorphous metal of the cover portion forms a cutting edge of said blade. To prevent multiple uses of the blade, the blade can be magnetically encoded upon its first use and rejected by the microkeratome machine if a subsequent use is attempted. However, the manufacturing process is complex and expensive.

Thus, there is a need in the art for a blade that can be manufactured in a simple fashion from inexpensive polymeric raw materials. Additionally, it is advantageous for the blade to be configured for one time use by virtue of its material composition.

SUMMARY OF THE INVENTION

The present invention provides a disposable blade for separating the epithelium of a cornea from the underlying Bowman's layer comprising a separator fabricated from a polymeric material. The separator comprises a front portion that includes a separating edge, a rear trailing portion having a rear edge, and a pair of side edges that extend from the front and rear portions. The separating edge is sharp enough to separate the epithelium layer from Bowman's layer, but not sharp enough to cut into Bowman's layer when in contact therewith. The blade may include a blade holder that is preferably, but not necessarily, a polymeric material.

In another aspect, the invention provides a separator to be used with a surgical device that separates the epithelium of a cornea from the underlying Bowman's layer of an eye of a patient, the surgical device including a positioning ring for temporary attachment to the eye and structured to present and expose the cornea to be separated, a separator head assembly structured and disposed to carry said separator, and a drive operably connected to the separator head assembly for causing movement of the separator across the positioning ring and for causing oscillating movement of said separator, said separator comprising a separating edge, said separator having a polymeric separating edge.

In a preferred aspect of the invention, the polymeric material of the separator is transparent. A transparent separator will not obstruct the visual field when observing the progress of the separator through the cornea. More preferably, the polymeric material comprises a slight tint so that there it is visibly different in perceived color than the epithelium.

In another preferred aspect, the separator is constructed of a polymeric material that will undergo dimensional changes if exposed to temperatures exceeding about 100 °C. This can be accomplished, for example, with a polymeric material that has a Vicat softening point below about 100 °C. This prevents the blade from being used after either autoclaving or steam sterilization, thus ensuring that a new, pristine blade is used on each patient. Only in this manner, can the quality and safety of the separator be guaranteed.

In yet another aspect of the present invention a method is provided for separating at least a portion of an epithelium from a cornea of an eye, so that an intact Bowman's layer is exposed. The method comprises the steps (a) fixing a positioning ring to an eye so that the cornea at least partially extends therethrough; (b) moving a separator having a polymeric separating edge along a travel path that intersects at least a portion of the cornea so as to separate the epithelium from the cornea, leaving Bowman's layer intact; and (c) retracting the separator out of contact with the cornea.

One object of the present invention is to provide a separator that is able to separate the epithelium of a cornea from the underlying Bowman's membrane in such a way that the epithelium can be easily and precisely aligned back into its original position following the reshaping of the cornea.

Another object of the present invention is to provide a separator that can be manufactured cheaply and easily such that the separator is disposable, thus reducing the chance of infection upon reuse after inadequate sterilization.

Yet another object of the present invention is to provide a separator that is incapable of being sterilized by autoclaving or steam sterilization after it has already been used one time. Such a separator should, however, be capable of being sterilized by other means, such as, for example, exposure to electromagnetic radiation, or to chemical agents.

A final object of the present invention is to provide a separator that does not obstruct the visual field of the surgeon as it progresses through the cornea.

Other objects, advantages, and salient features of the present invention will become apparent from the following detailed description, which, taken in conjunction with the annexed drawings, discloses preferred embodiments of the invention.

DESCRIPTION OF THE FIGURES

Fig. 1 is a diagram showing a perspective view of a separator according to one embodiment.
FIG. 2 is a cross-sectional view of the first three layer of tissue of the cornea of an eye.
Fig. 3 is a diagram showing a partial side view of a separator's flat leading edge according to an embodiment.
Fig. 4 is a diagram showing a partial side view of a separator's rounded leading edge according to another embodiment.
Fig. 5 is a diagram showing a partial side view of a separator's angled leading edge according to yet another embodiment.
Figs. 6A – 6C are diagrams showing cross sectional views of separators according to different embodiments.
FIG. 7 is a diagram showing a side view of a separator assembly according to the present invention.
FIG. 8 is a diagram showing a side view of a hand piece useful in practicing the present invention.

FIG. 9 is a side view of the separator assembly in a first position slidably engaged with a hand piece secured to the eye by vacuum.
FIG. 10 is a side view of the separator assembly in a second position slidably engaged with a hand piece secured to the eye by vacuum.
FIG. 11 is a side view of the separator assembly in a third position slidably engaged with a hand piece secured to the eye by vacuum.
FIG. 12 is a top view of portions of the hand piece and separator assembly after the epithelium has been separated from the eye.
FIG. 13 is a cross sectional side view of a portion of the separator assembly showing the spatial relationship between the separating edge and the applanator.
FIGs. 14A – 14C show the various placements of the separated epithelium as the separating edge engages the cornea and causes separation of the epithelium for Bowman's layer.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

The disclosed epithelium separator is especially suited for use in excimer laser reshaping of the cornea. It is safer than standard microkeratomes used in eye surgery, and is inexpensive enough to be a disposable, single use device, which eliminates the need for sterilization between procedures, and thus reduces the possibility of infection.

The disclosed separator is ideally suited to the unique requirements for separating the epithelium layer from the underlying Bowman's layer. While microkeratomes developed to sever the stroma for laser in situ keratomileusis were required to be extremely hard and sharp to maintain a radius of curvature as low as 1 micron at the edge, the present separator has no such stringent requirements and can be constructed of cheaper, softer materials. In fact, the edge of the separator cannot be so sharp as to sever Bowman's layer under normal operating conditions, but instead, only has sharpness sufficient to cleave the boundary between the epithelium and Bowman's layer.

Referring to FIG. 1, the separator 100 comprises a separator body 102 having a separating edge 104, a rear edge 106, and a pair of side edges 108, 110 that extend from the separating edge 104 to the rear edge 106 defining the body. In a preferred embodiment, the plane of the rear edge 106 is generally parallel to the line of separating edge 104. The

separating edge 104 is the first portion of the separator 100 to come into contact with the cornea and effects the separation of the epithelium therefrom.

While the dimensions and configuration of the separator are largely determined by the instrument in which they are to be used, the separator 100 is preferably less than 1000 microns in thickness. However, because the separating edge 104 must not be sharp enough to cut into Bowman's layer under normal operating conditions, it should not be so thin that excision of Bowman's layer would occur. The separating edge 104 is preferably greater than about 200 microns.

While the separator 100 can be flat, having a rear edge 106 substantially the same width as the separating edge 104, more preferably, the rear edge 106 is thicker in dimension than the separating edge 104. In some cases, the rear edge 106 may be an order of magnitude thicker than the separating edge 104, and even up to two orders of magnitude thicker. Such dimensions may make it easier for the surgeon to handle the separator prior to insertion into the surgical device and also aid in its stability once installed.

The cornea 200 of the human eye includes five layers, the outer three of which are illustrated in FIG. 2. The outer most layer is known is as the epithelium layer 202 and is typically 50 to 90 microns thick. The epithelial layer 202 is stratified, possessing 5 to 6 layers of epithelial cells, which are held together by desmosomes (not shown). Bowman's membrane 204 separates the epithelium from the stroma layer 206. Bowman's membrane 204 is typically about 12 microns thick, while the stroma 206 is from 400 to 450 microns thick and makes up most of the thickness of the cornea. While the preferred embodiment of the present invention is considered optimal for use upon a human eye, it is understood that such a separator is useful for use on similar animal eyes, including eyes of most mammals and many vertebrates, such as horses, dogs, cats, elephants, sheep, and swine.

In Fig. 3 shows a side view of a flat separating edge 302 of a separator 100 according to one embodiment. The polymeric separating edge 302 of the separator 100 should not be too wide such that it will reduce the consistency with which the epithelial layer 202 is penetrated. The separating edge 302 preferably is about 5 to 25 micrometers thick, and more preferably about 15 micrometers thick. Fig. 4 shows a side view of a rounded separating edge 402 according to another embodiment of the separator 100. As shown in FIG. 5, the separating

edge can also come to an angled point 502, provided, however, that it is not sufficiently sharp to sever Bowman's layer when used as intended.

As demonstrated in FIG. 6A, the separator 600 need not be the flat rectangular shape shown in FIG. 1. The preferred separator 600 comprises a separator body 602 having a polymeric separating edge 604, a rear edge 606, and a pair of side edges (not shown) that extend from the polymeric separating edge 604 to the rear edge 606 defining the body. The notch 605 on the underside of the separator 600 interacts with a support member 703 (see Fig. 13) for stability.

While the separator 600 of FIG. 6A has been described as being a solid body of polymeric material, and optionally including reinforcing material therein, in particular embodiments, a separator 600 may be fabricated as a polymeric coated metallic or ceramic body. For example, a metallic core 618 may be employed as a base upon which the polymeric or polymeric-composite material 616 may be disposed. While FIG. 6C, shows a polymeric coating 616 over only the separating edge, the coating 616 may cover the entire metallic core 618. In this manner, the metal core will provide rigidity to the separator 600 whereas the polymeric material 616 will provide the separating edge 614 for contact with the cornea.

FIG. 6B shows an alternative embodiment of the present invention in which the separator 600 comprises a polymeric front portion 610 that includes a separating edge 612, and a metallic rear portion 608 comprising a rear edge 609. The front portion 610 is joined to the rear portion 608 in any one of a variety of known ways. As in the embodiment shown in FIG. 6B, the metal portion 608 will provide rigidity to the separator 600 whereas the polymeric portion 610 will provide the separating edge 612 for contact with the cornea.

Referring to FIGS. 7 – 9 and 12, one embodiment of the surgical device of the present invention comprises a hand piece 800 with an integral vacuum ring 802 and a separator assembly 700. (Note that, for simplicity, the separator cover 706 is not shown in FIGS. 9 – 11 and that the figures are not necessarily drawn to scale.) Separator assembly 700 comprises a drive shaft 710 that engages a motor (not shown) through a bushing 806 in the hand piece 800 to move the separator assembly 700 transversely and to oscillate the separator 600. Vacuum is applied to the vacuum ring 802 through vacuum port 804 to secure the eye thereto.

Preferably, one or more motors (not shown) provide two types of motion to the separator assembly 700 and the separator 600. The first type of motion is side-to-side oscillation along an axis parallel to the separating edge 604 of the separator 600 to assist in the separation process. The second type of motion is longitudinal motion perpendicular to the separating edge 604 of the separator 600 to advance the separation along the cornea. The rotational motion of the motor is transferred from the drive shaft 710 to the plunger assembly 712, through which it is translated to oscillations in the separator 600. Under action from the plunger assembly 712, the separator 600 is oscillated by the motor. The separator 600 can oscillate either transversely, vertically, or longitudinally with frequency ranging from about 10 Hz to about 10 KHz. Electromagnetic or piezoelectric forces on the separator 600 can alternatively provide the oscillation, or external rotating or vibrating wires can provide the oscillation. The separator 600 is preferably oscillated along the separator support 703 in a direction perpendicular to the plane of the figure.

Applanator 702 is connected to the separator assembly 700 in a position forward of the separator 600. Separator 600 is held firmly within the separator assembly 700 by separator cover 706, which is preferably hingedly connected to the hand piece 700 moveable in the direction of the arrow in FIG. 7. The cover 706 is secured in place through a locking screw 708, which can be tightened by hand through the locking screw head 704.

Separator assembly 700 is slidably associated with hand piece 800 through grooves 1208a, 1208b. Fig. 9 shows a cross sectional side view of an eye 902 of a patient and an epithelial separator device comprising the hand piece 800 associated with the separator assembly 700. When the eye 902 is placed within the vacuum ring 802 and a vacuum is applied to vacuum port 804, the surface of the eye 902 is tightened and pulled through the ring 802 to expose the cornea 200 at a position forward of the applanator 702. As shown in FIG. 9, the separator assembly 700 begins in a first position located away from the eye 902.

Referring now to FIG. 10, as the applanator 702 moves forward under action of the drive shaft 700 through tracks 1208a, 1208b, the cornea 200 is forced against the undersurface of the applanator 702. This results in a flattening of the cornea 200 before it comes into contact with the separator 600. As the separator assembly 600 moves along the cornea 200 of the eye 902, the separator 600 engages the cornea 200 and removes the epithelium layer

202 located at the surface of the cornea 200 of the eye 902. However, the separator 600 is not sharp enough to excise Bowman's layer 204 during operation of the epithelial separator device.

Referring now to FIG. 13, the separating edge 604 is positioned or angled such that it is a height h below the bottom surface of the applanator 702. The distance from the separating edge and the bottom surface of the applanator does not determine the depth of the cut, as in prior art LASIK procedures. Therefore, the exact value of this distance is not as critical to performance of the separator as it was to LASIK procedures where tens of microns can be the difference between a successful flap and a medical emergency. While prior art LASIK microkeratomes typically cut at a distance of 130 – 150 microns, the present separator can be set at a depth (h) from between 40 microns to 300 microns, more preferably from 40 to 100 microns. Surprisingly, consistent epithelium removal has been demonstrated at depths of about 240 microns.

The separator 600 is fabricated from a synthetic polymeric material. The preferred polymeric material is a thermoplastic or thermoset polymer or ionomer. There are presently available a wide variety of durable, resilient polymers which may be employed to fabricate the separator. Included among such materials are, but are not limited to, acetals, (meth)acrylates, acrylics, alkyds, polycarbonates, polyolefins, polyesters and co-polyesters, polymethylpentene, polypropylene, polysulfones, cellulosics, styrene acrylic co-polymers, fluoropolymers, nylons, polystyrene, polyetheretherketones (PEEK), polyarylates, polyetherimides, styrene acrylonitrile, silicones, epoxys, polyvinyl chloride, urethanes, acrylonitrile-butadiene-styrene (ABS), methylmethacrylate-acrylonitrile-butadiene-styrene (MABS), allyl diglycolcarbonate, as well as combinations or blends of these polymers. The preferred polymeric materials are polycarbonates, PEEK, polystyrenes, MABS, acetal homopolymers, and poly(methyl methacrylate) (PMMA). It has in fact been found, in accord with the principles of the present invention, that many of these materials can retain a sufficiently sharp edge and have sufficient durability and resiliency to function as a separator.

Preferably, the separator has a flexural modulus of at least about 1.5 GPa according to ASTM D790-02, more preferably at least about 2.0 GPa, and most preferably at least about 3.0 GPa. Furthermore, the separator preferably has a tensile strength at yield of at least about 25 MPa according to ASTM D638-02, more preferably at least about 40 MPa, and

most preferably at least about 50 MPa. Additionally, the separator preferably has either a Rockwell M hardness greater than or equal to 70 or a Rockwell R hardness greater than or equal to 90, according to ASTM D785-98e1. Most preferably, the material has a Rockwell M hardness of greater than 90. Such relatively stiff materials (compared to other plastics) are preferred in order to avoid deformation of the separator during normal operation. However, it is indeed surprising that such materials having strength and hardness less than stainless steel are nonetheless suitable for use in a separator in the present invention. Commercially available materials meeting the above preferred criteria include various grades and formulations of PEEK, PMMA, acetal homopolymer, polystyrene, MABS, and polycarbonate.

In addition to the stiffness of the material, the toughness of the material can be important in the use of the separator. Accordingly, the separator preferably has a toughness of at least about 1 J/cm^2, more preferably at least about 2 J/cm^2, most preferably at least about 3 J/cm^2, according to ISO 179-1 (15 Dec 2000) Charpy Impact Test. When this test method is referenced to herein it is meant to refer only to the portion of the test performed at 23 °C using unnotched specimens. Such relatively tough materials (compared to other plastics) are preferred in order to avoid cracking or shattering of the separator during normal operation. However, it is indeed surprising that such materials having toughness less than stainless steel are nonetheless suitable for use in a separator in the present invention. Commercially available materials meeting the above preferred criteria include various grades and formulations of PEEK, PMMA, acetal homopolymer, polystyrene, MABS, and polycarbonate. However, while unmodified polystyrene has moderate strength, it is rigid and brittle. Impact strength is increased significantly by blending the polymer with rubbers such as polybutadiene. The preferred MABS is available commercially for BASF as Terlux® 2802 and the preferred polystyrene is commercially available from Nova Chemicals as Crystal PS 3500. Table 1 below presents data provided by the manufacturer of various polymers.

TABLE 1

	Tensile Strength at Yield (MPa)	Flexural Modulus (GPa)	Charpy Impact (J/cm^2)	Vicat Softening (°C)
Terlux® 2802	48	*	15	91
Crystal PS 3500	36	3.5	*	92
Victrex PEEK 450G	97	4.1	*	*
BASF Lucryl® KR 2008/1 PMMA	60	*	5	106

* Data not provided by manufacturer

In another embodiment, the polymeric material is reinforced by incorporation of various inorganic filler materials. For example, carbon and glass fibers and powders have been incorporated into various polymeric materials to greatly increase flexural strength. Such materials typically have high degrees of strength and are capable of taking and maintaining a sufficient separating edge, as well as providing sufficient toughness to allow for their use in fabricating the separating device.

In yet another embodiment of the invention, the polymeric material of the separator is transparent. A transparent separator will not obstruct the visual field when observing the progress of the separator through the cornea. The polymeric material preferably exhibits a light transmission greater than 50 percent, more preferably greater than 75 percent, and a haze factor less than about 25 percent, more preferably less than about 5 percent, in accordance with ASTM D1003-00. More preferably, the polymeric material comprises a slight tint so that there it is visibly different in perceived color than the epithelium. This is easily accomplished, for example, by addition of a tinting agent to the polymer before manufacture. The slight tint will provide a contrast between the blade and the epithelium enabling the surgeon to differentiate therebetween, but yet, still providing optical clarity for observation of the cornea during use. The tint, by increasing the visibility of the separator during use, will also make it easier for the surgeon to handle the blade prior to insertion into the surgical device.

The tinting agent can include one or more pigments. Preferably, the pigment is a white pigment, a black pigment, a blue pigment, a brown pigment, a cyan pigment, a green

pigment, a violet pigment, a magenta pigment, a red pigment, or a yellow pigment, or shades or combinations thereof. Suitable classes of colored pigments include, for example, anthraquinones, phthalocyanine blues, phthalocyanine greens, diazos, monoazos, pyranthrones, perylenes, heterocyclic yellows, quinacridones, diketopyrolo-pyroles, and (thio) indigoids. Representative examples of phthalocyanine blues include copper phthalocyanine blue and derivatives thereof (Pigment Blue 15). Representative examples of quinacridones include Pigment Orange 48, Pigment Orange 49, Pigment Red 122, Pigment Red 192, Pigment Red 202, Pigment Red 206, Pigment Red 207, Pigment Red 209, Pigment Violet 19 and Pigment Violet 42. Representative examples of anthraquinones include Pigment Red 43, Pigment Red 194 (Perinone Red), Pigment Red 216 (Brominated Pyanthrone Red) and Pigment Red 226 (Pyranthrone Red). Representative examples of perylenes include Pigment Red 123 (Vermillion), Pigment Red 149 (Scarlet), Pigment Red 179 (Maroon), Pigment Red 190 (Red), Pigment Violet, Pigment Red 189 (Yellow Shade Red) and Pigment Red 224. Representative examples of thioindigoids include Pigment Red 86, Pigment Red 87, Pigment Red 88, Pigment Red 181, Pigment Red 198, Pigment Violet 36, and Pigment Violet 38. Representative examples of heterocyclic yellows include Pigment Yellow 1, Pigment Yellow 3, Pigment Yellow 12, Pigment Yellow 13, Pigment Yellow 14, Pigment Yellow 17, Pigment Yellow 65, Pigment Yellow 73, Pigment Yellow 74, Pigment Yellow 110, Pigment Yellow 117, Pigment Yellow 128, Pigment Yellow 138, and Pigment Yellow 151. A representative example of diketopyrolo-pyroles include Pigment Red 254. Such pigments are commercially available in either powder or press cake form from a number of sources including, BASF Corporation, Engelhard Corporation and Sun Chemical Corporation. Examples of other suitable colored pigments are described in the Colour Index, 3rd edition (The Society of Dyers and Colourists, 1982).

In another preferred embodiment, the separator is constructed of a polymeric material that will undergo dimensional changes if exposed to temperatures exceeding about 121 °C, most preferably exceeding about 100 °C. Such a material is incapable of being autoclaved after use, thereby ensuring that separators are not reused. More preferably, the polymeric material has a Vicat softening point, measured by ASTM D1525-00 of less than about 121 °C, most preferably less than about 100 °C. The Vicat softening point is the temperature at which a flattened needle of 1 mm^2 cross section, and under a specified constant load, penetrates a specimen of the plastic to a depth of 1 mm. It is useful as a rough comparative guide to a resin's resistance to elevated temperatures.

Referring to Fig. 14A, the separator 600 is used with a surgical device that separates the epithelium 1206 of a cornea from the underlying Bowman's layer 204 of an eye of a patient. As the separator 600 is positioned in contact with the eye, the separator edge 604 will cleave the fibrils connecting the epithelium 1206 to Bowman's layer 204, but will not slice into Bowman's layer 204. The separator 600 pushes the epithelial cells 1206 and preferably, does not exert a force that could disrupt the intercellular bonds, such as the desmosomes. As the separator edge 604 progresses along the eye, the epithelium 1206 is preferably left free to assume an unhindered position and configuration. Often, the epithelium 1206 will progress along the top surface of the applanator 702. Referring to FIG. 14B, depending, in part, on the angle of incidence of the separator 600 and the depth of encounter (h), the epithelium 1206 may be pushed out in front of the separator 600, forming multiple folds 1400a, 1400b as it progresses. Alternatively, the epithelium may progress up the front surface 1402 of the separator 600 as shown in FIG. 14C.

By not constraining the epithelium 1206 during separation, the epithelium 1206 encounters minimal stress and strain and will suffer less cell death. This is particularly important when the separator 600 is oscillated. If the epithelium 1206 is constrained or otherwise prevented from moving freely (such as being held against a surface post-separation), the oscillatory energy of the separator 600 will be absorbed, at least partially, by the epithelium 1206, causing cell disruption or death. However, a freely moving epithelium 1206 will not absorb as much energy from the oscillatory movement of the separator 600 and will maintain structural integrity.

Referring back to FIG. 12, when the separator assembly 700 is retracted from the cornea after separation as occurred, the separated epithelium layer 1206 is preferably left partially attached to the cornea of the eye by a hinge 1202. The hinge 1202 is preferably about 1 cm in length, but can differ significantly from this, provided enough of Bowman's layer 1204 is exposed to perform laser ablation. The separated epithelium 1206 typically will be laid out flat upon the exposed Bowman's layer 1204 after the separator assembly 700 is retracted. In this case, the epithelium is carefully moved to the side with forceps to the position shown prior to laser ablation. The applanator 702 is not shown here for more clarity of the drawing.

While the invention has been described above by reference to various embodiments, it will be understood that many changes and modifications can be made without departing from the scope of the invention. It is therefore intended that the foregoing detailed description be understood as an illustration of the presently preferred embodiments of the invention, and not as a definition of the invention. It is only the following claims, including all equivalents, which are intended to define the scope of this invention.

We Claim:

1. A separator to be used with a surgical device that separates the epithelium of a cornea from the underlying Bowman's layer of an eye of a patient, the surgical device including a positioning ring for temporary attachment to the eye and structured to present and expose the cornea to be separated, a separator assembly structured and disposed to carry said separator across the positioning ring, said separator having a polymeric separating edge that separates the epithelium of the cornea from the underlying Bowman's layer when brought into contact with the eye as the separator moves across the positioning ring.

2. A separator as claimed in Claim 1, where said separating edge is not sufficiently sharp to sever Bowman's layer when brought into contact with the eye.

3. A separator as claimed in Claim 1, wherein said polymeric separating edge comprises a polymeric material selected from the group consisting of acetals, (meth)acrylates, acrylics, alkyds, polycarbonates, polyolefins, polyesters and co-polyesters, polymethylpentene, polypropylene, polysulfones, cellulosics, styrene acrylic co-polymers, fluoropolymers, nylons, polystyrene, polyetheretherketones (PEEK), polyarylates, polyetherimides, styrene acrylonitrile, silicones, epoxys, polyvinyl chloride, urethanes, acrylonitrile-butadiene-styrene (ABS), methylmethacrylate-acrylonitrile-butadiene-styrene (MABS), allyl diglycolcarbonate, and combinations thereof.

4. A separator as claimed in Claim 3, wherein said polymeric material is selected from the group consisting of polycarbonates, PEEK, polystyrenes, MABS, acetal homopolymers, and PMMA.

5. A separator as claimed in Claim 1, wherein said polymeric separating edge comprises a polymeric material having a flexural modulus of at least about 1.5 GPa according to ASTM D790.

6. A separator as claimed in Claim 1, wherein said polymeric separating edge comprises a polymeric material having a tensile strength at yield of at least about 25 MPa according to ASTM D638.

7. A separator as claimed in Claim 1, wherein said polymeric separating edge comprises a polymeric material having either a Rockwell M hardness greater than or equal to 70 or a Rockwell R hardness greater than or equal to 90, according to ASTM 785.

8. A separator as claimed in Claim 1, wherein said polymeric separating edge comprises a polymeric material having a toughness of at least about 1 J/cm^2, according to ISO 179 Charpy Impact Test, unnotched at 23 °C.

9. A separator as claimed in Claim 1, wherein said polymeric separating edge comprises a polymeric material and an inorganic filler material selected from the group consisting of carbon powder, carbon fibers, glass powder, and glass fibers.

10. A separator as claimed in Claim 1, wherein said polymeric separating edge comprises a transparent polymeric material.

11. A separator as claimed in Claim 10, wherein said transparent polymeric material having a light transmission greater than 50 percent, and a haze factor less than about 25 percent, in accordance with ASTM D1003.

12. A separator as claimed in Claim 11, wherein said transparent polymeric material further comprises a tinting agent.

13. A separator as claimed in Claim 1, wherein said polymeric separating edge comprises a polymeric material having a Vicat softening point, measured by ASTM D1525, of less than 120 °C.

14. A separator comprising a polymeric separator body having a separating edge, a rear edge, and a pair of side edges that extend from the separating edge to the rear edge, wherein said separating edge is brought into contact with a cornea of an eye the epithelium of the cornea separates from the underlying Bowman's layer and said separator will not cut into the Bowman's layer.

15. A separator as claimed in Claim 14, wherein said polymeric material selected from the group consisting of acetals, acrylics, alkyds, polycarbonates, polyesters and co-polyesters,

polymethylpentene, polypropylene, polysulfones, cellulosics, styrene acrylic co-polymers, fluoropolymers, nylons, polystyrene, polyetheretherketones (PEEK), polyarylates, polyetherimides, styrene acrylonitrile, silicones, epoxys, polyvinyl chloride, urethanes, acrylonitrile-butadiene-styrene (ABS), methylmethacrylate-acrylonitrile-butadiene-styrene (MABS), allyl diglycolcarbonate, and combinations thereof.

16. A separator as claimed in Claim 15, wherein said polymeric material is selected from the group consisting of polycarbonates, PEEK, polystyrenes, MABS, acetal homopolymers, and PMMA.

17. A separator as claimed in Claim 14, wherein said polymeric material has a flexural modulus of at least about 1.5 GPa according to ASTM D790.

18. A separator as claimed in Claim 14, wherein said polymeric material has a tensile strength at yield of at least about 25 MPa according to ASTM D638.

19. A separator as claimed in Claim 14, wherein said polymeric material has either a Rockwell M hardness greater than or equal to 70 or a Rockwell R hardness greater than or equal to 90, according to ASTM 785.

20. A separator as claimed in Claim 14, wherein said polymeric material has a toughness of at least about 1 J/cm2, according to ISO 179 Charpy Impact Test, unnotched at 23 °C.

21. A separator as claimed in Claim 14, wherein said polymeric material further comprises an inorganic filler material selected from the group consisting of carbon powder, carbon fibers, glass powder, and glass fibers.

22. A separator as claimed in Claim 14, wherein said polymeric material is transparent.

23. A separator as claimed in Claim 22, wherein said polymeric material has a light transmission greater than 50 percent, and a haze factor less than about 25 percent, measured in accordance with ASTM D1003.

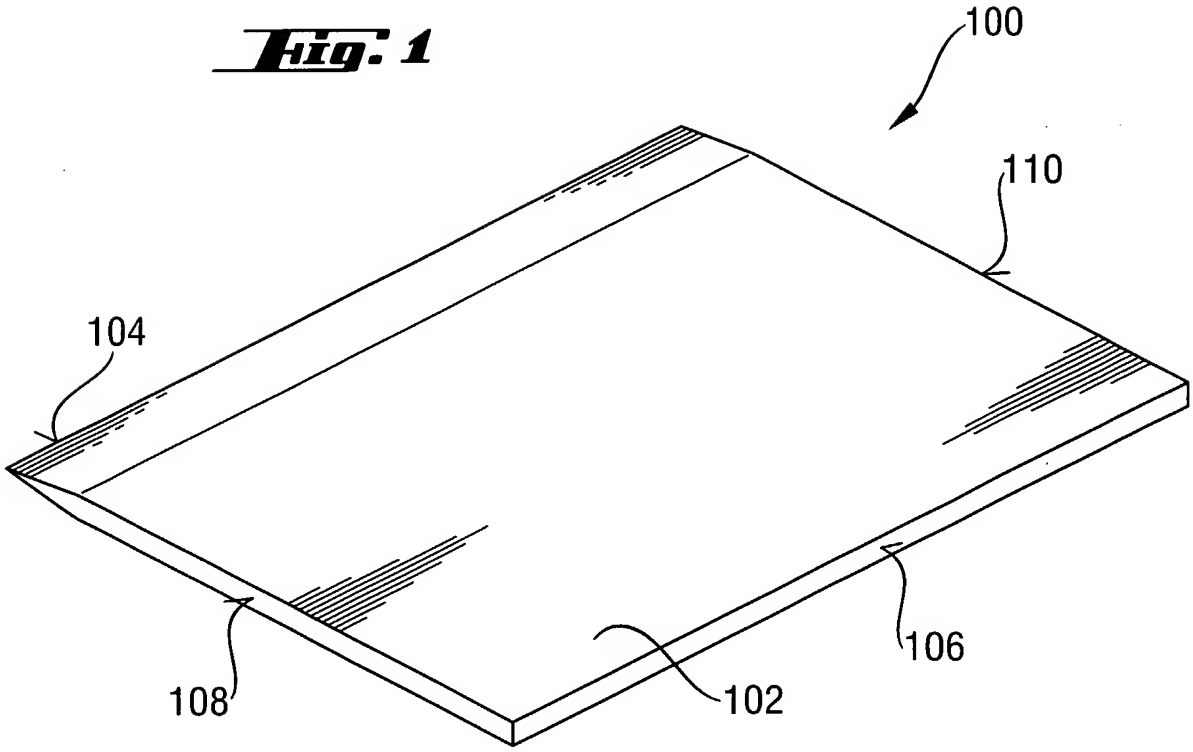
24. A separator as claimed in Claim 23, wherein said polymeric material further comprises a tinting agent.

25. A separator as claimed in Claim 14, wherein said polymeric material has a Vicat softening point, as measured by ASTM D1525, of less than 120 °C.

26. A method for separating at least a portion of an epithelium from a cornea of an eye, so that an intact Bowman's layer is exposed, comprising the steps of:
(a) fixing a positioning ring to an eye so that the cornea at least partially extends therethrough;
(b) moving a separator having a polymeric separating edge along a travel path that is generally parallel to the positioning ring and intersects at least a portion of the cornea so as to separate the epithelium from the cornea, leaving Bowman's layer intact; and
(c) retracting the separator outside the positioning ring.

27. A method as claimed in Claim 26, further comprising the step of flattening at least a portion of the cornea prior to moving the separator along the travel path.

Fig. 1



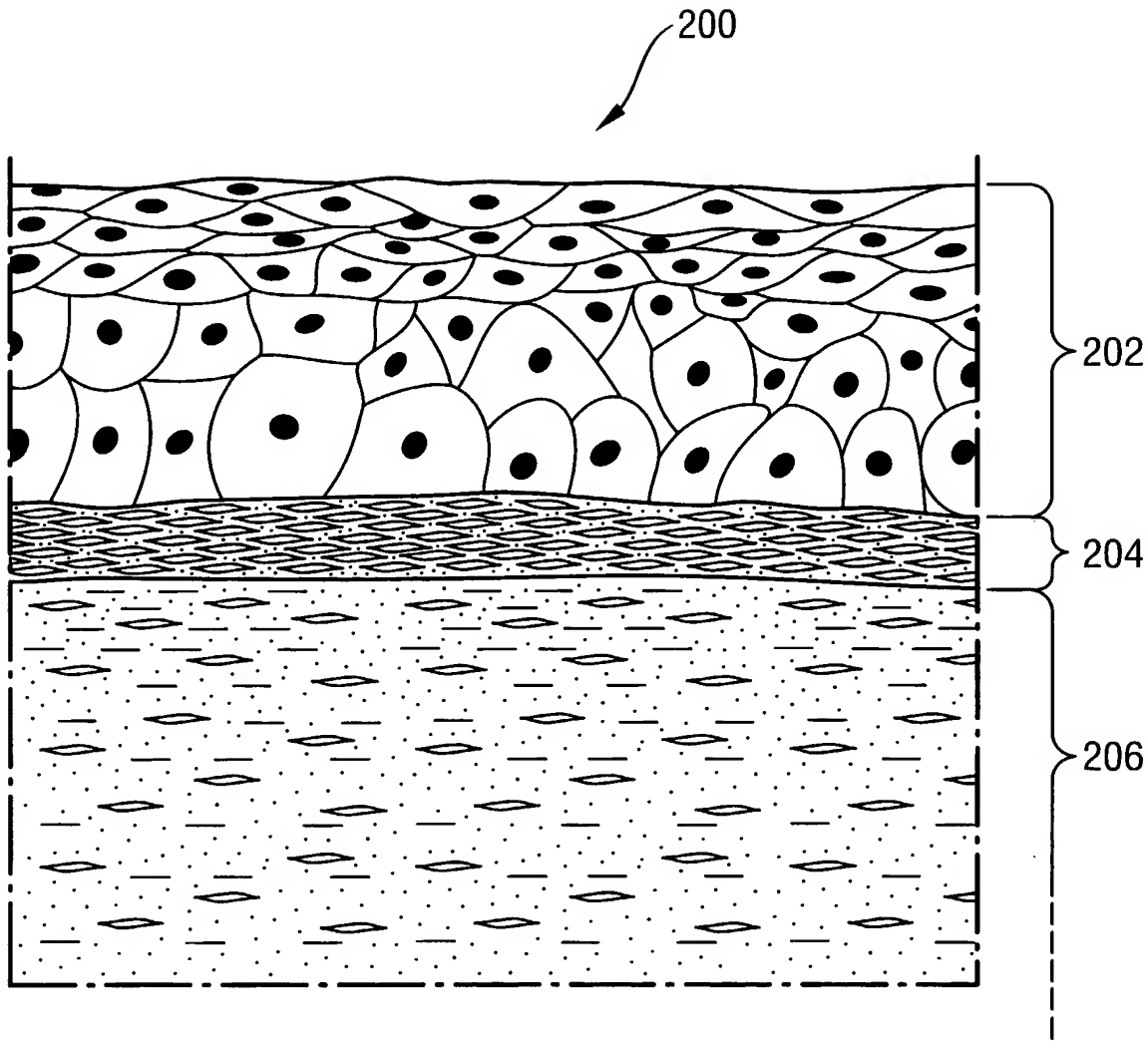


Fig. 2

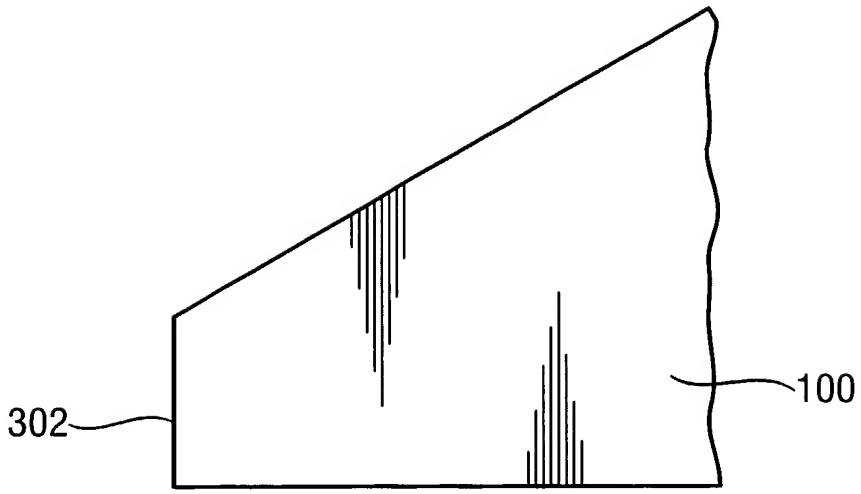


Fig. 3

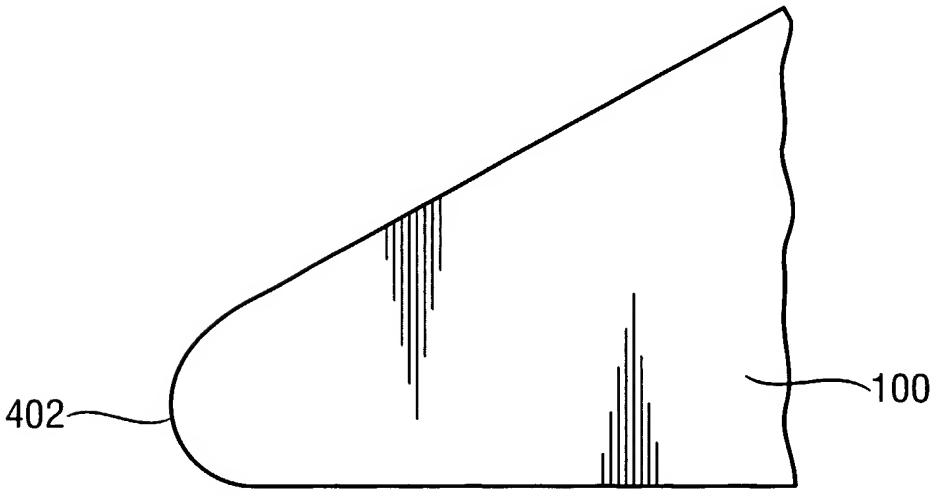


Fig. 4

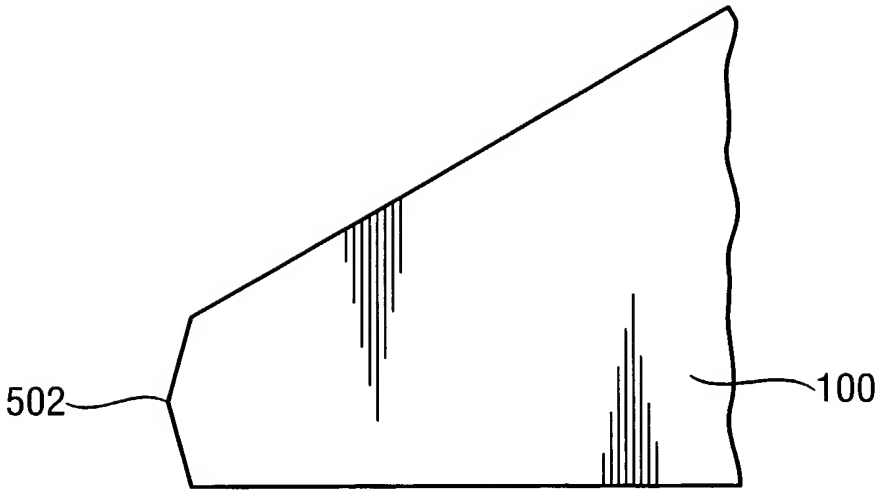


Fig. 5

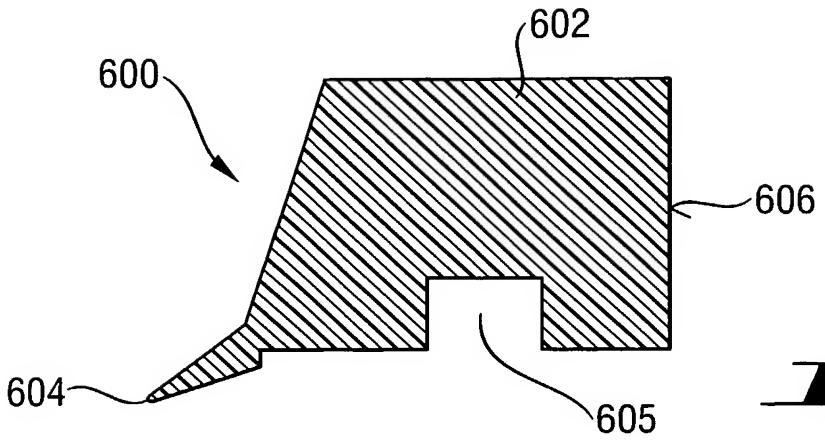


Fig: 6A

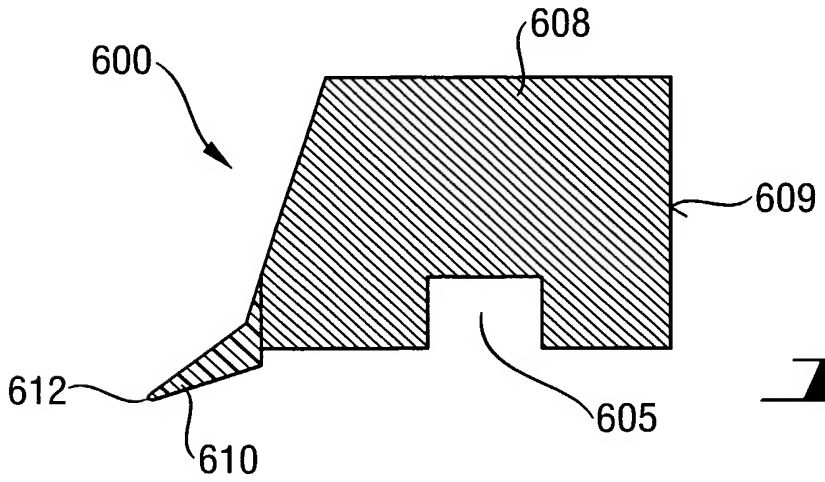


Fig: 6B

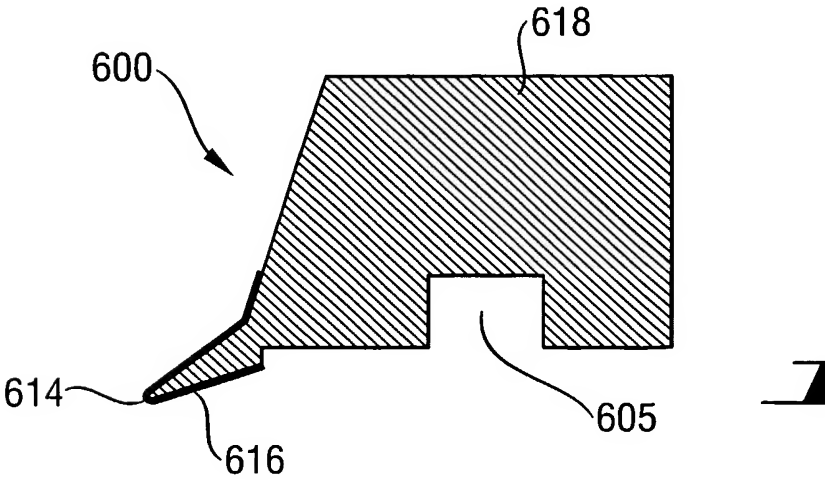


Fig: 6C

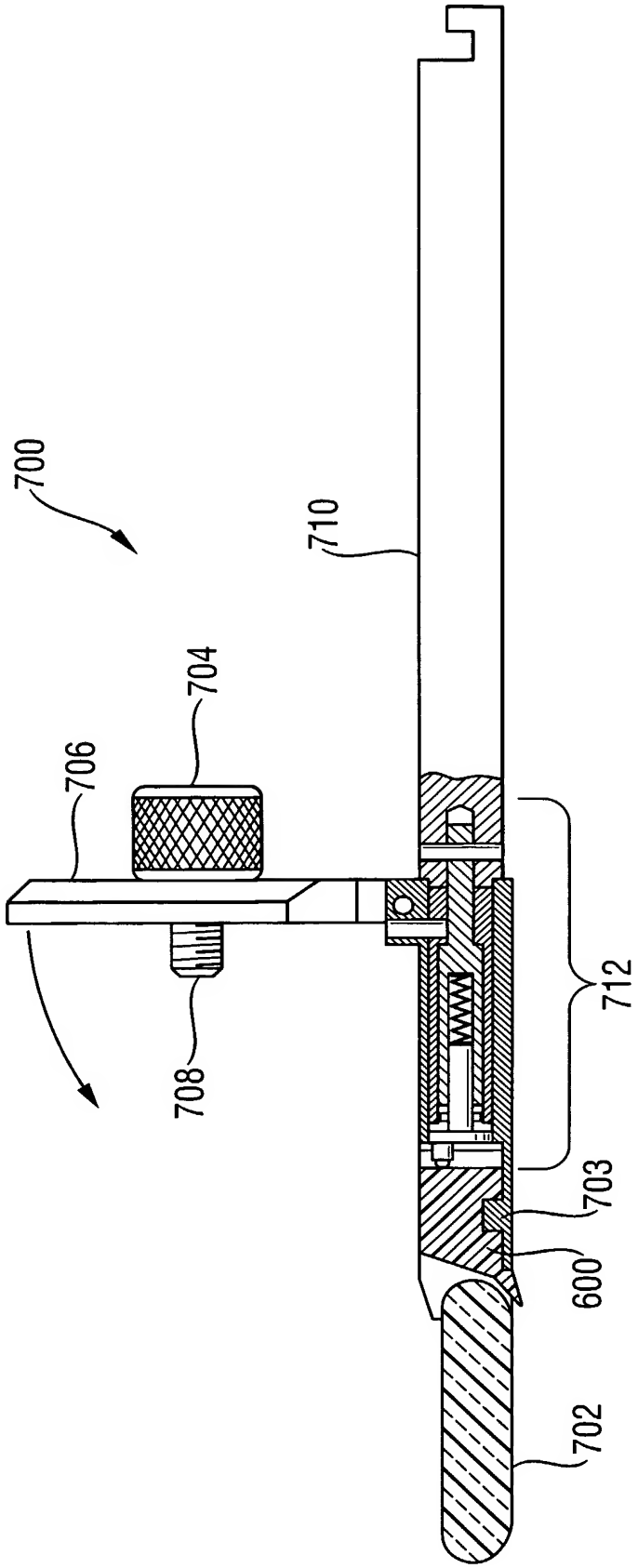


Fig. 1

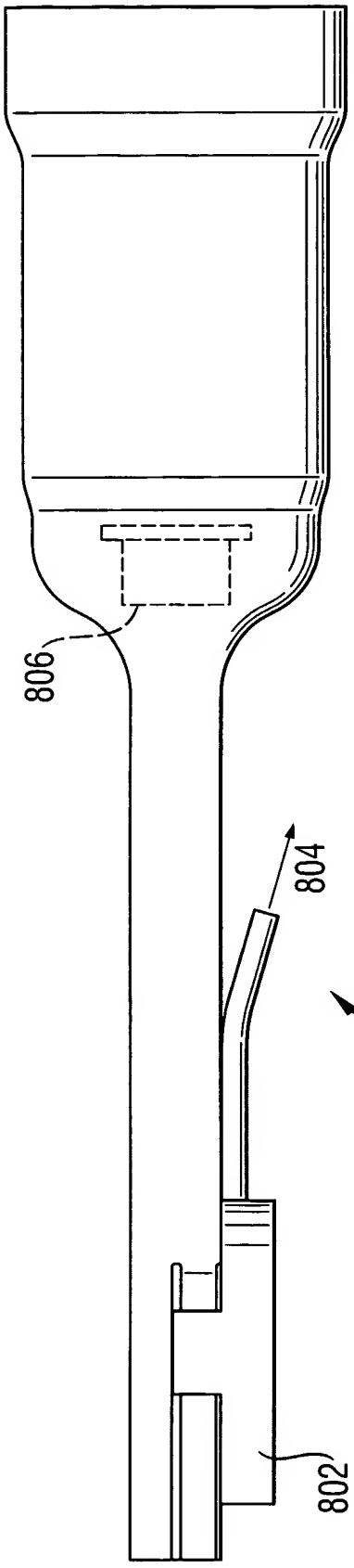


Fig. 8

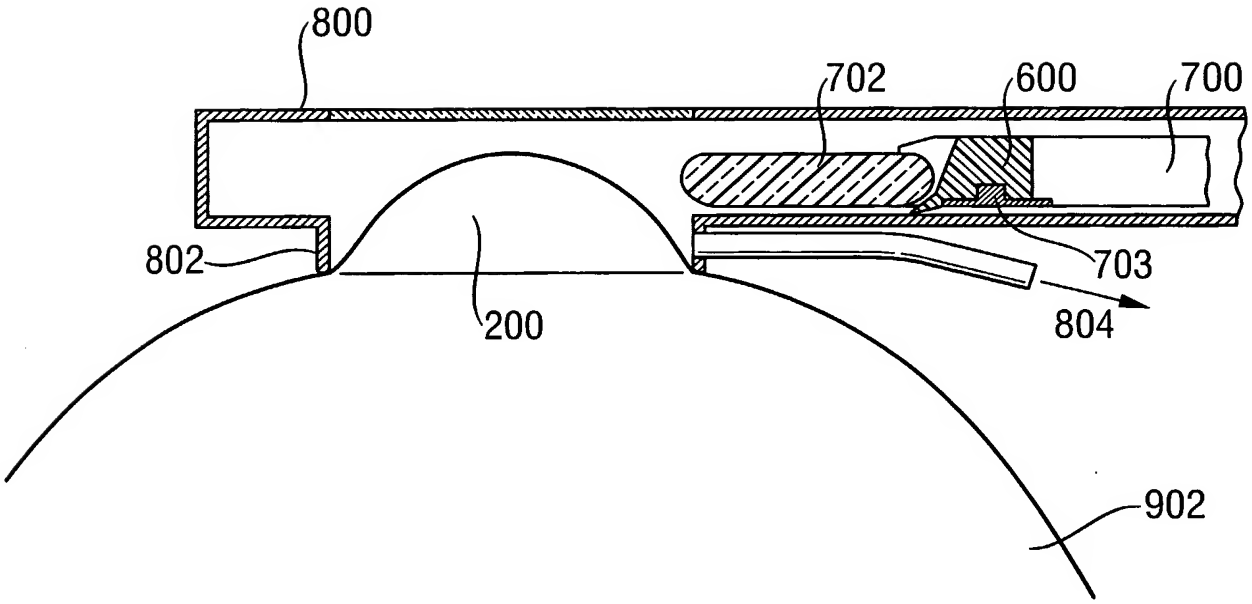


Fig: 9

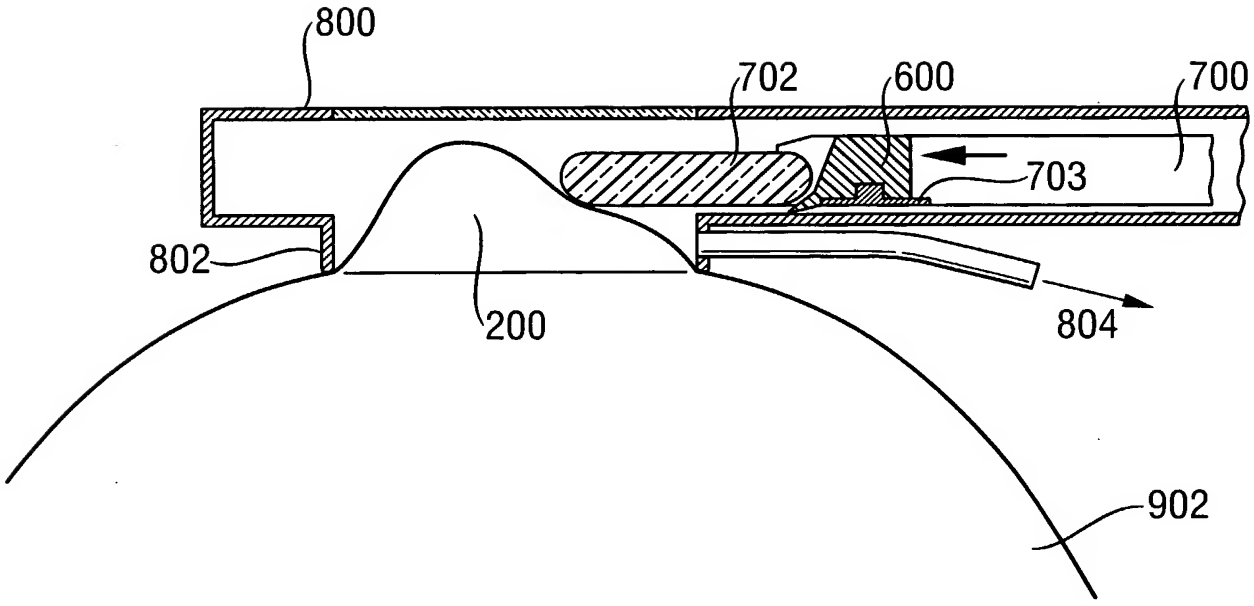


Fig: 10

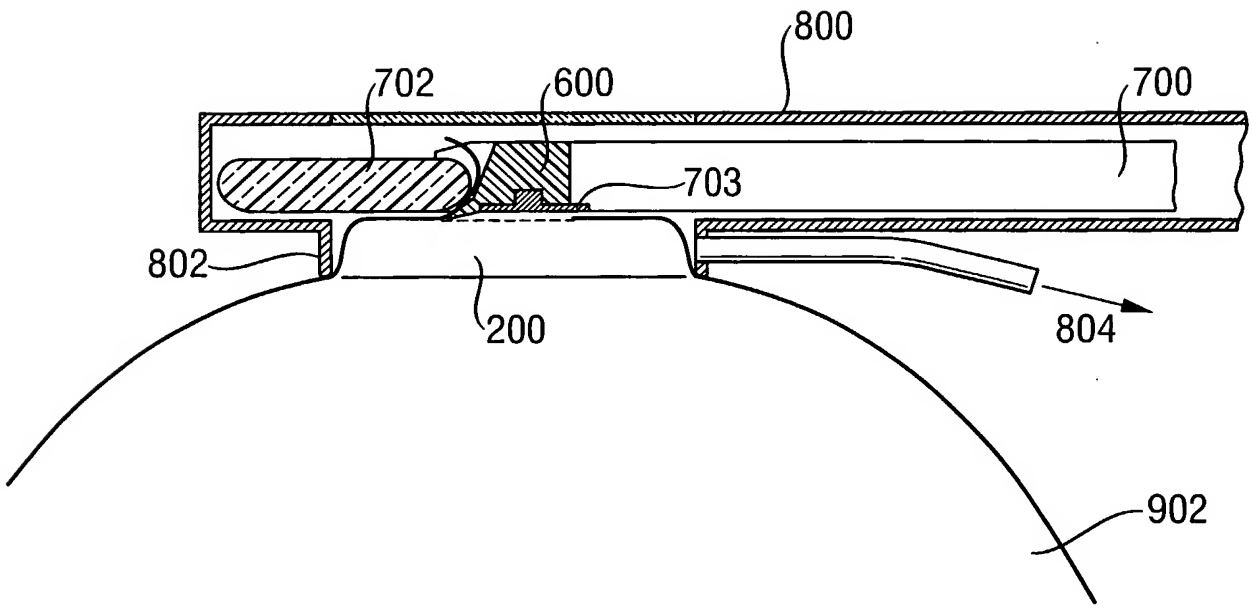


Fig. 11

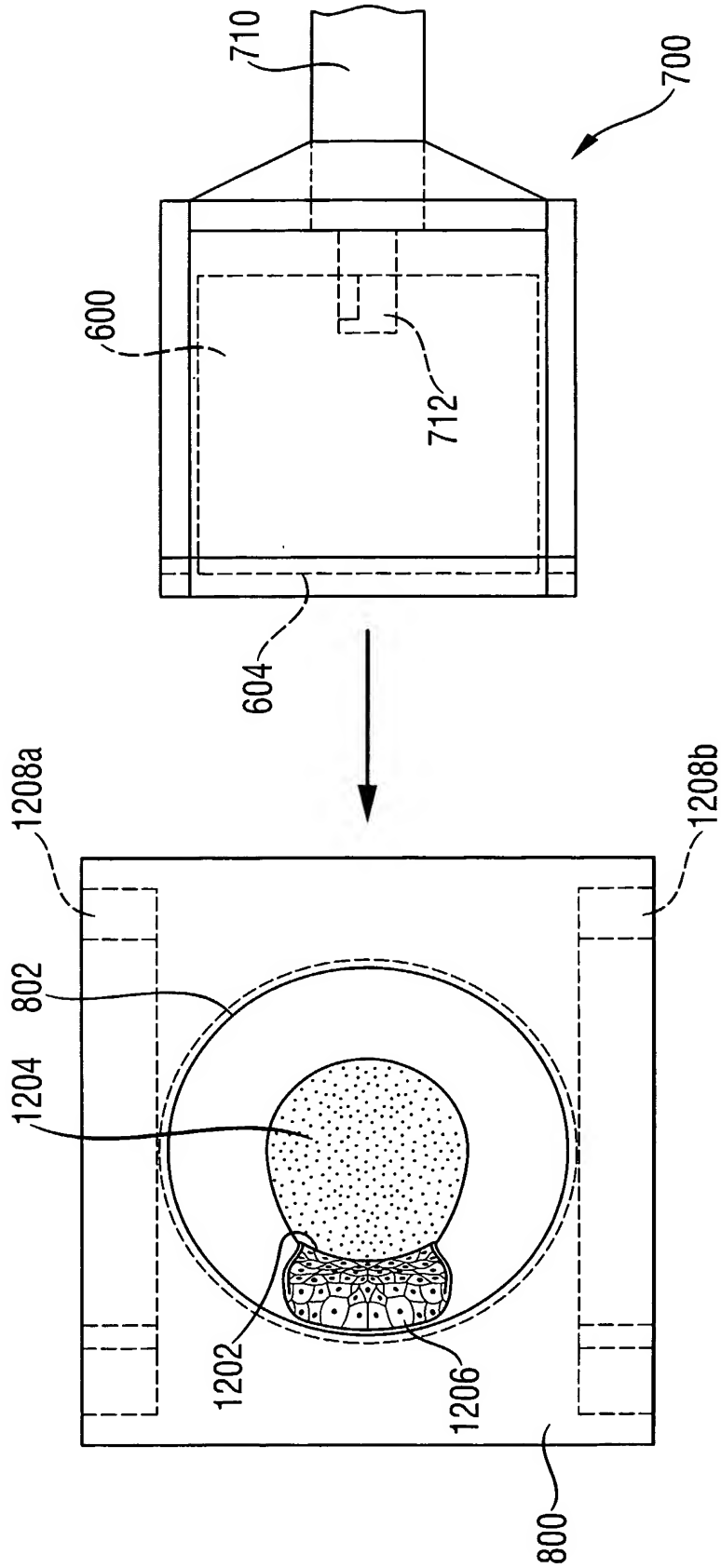


Fig. 12

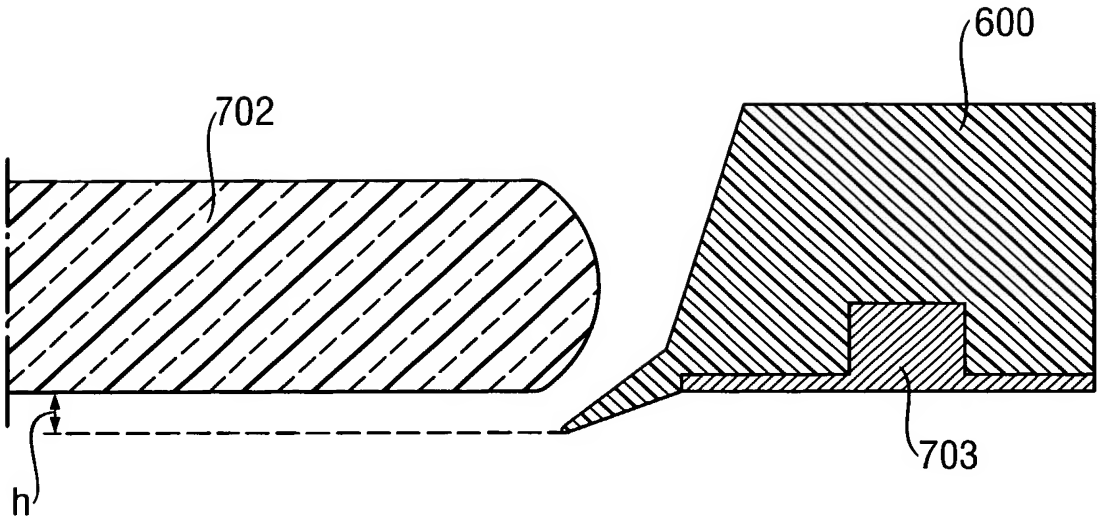


Fig. 13

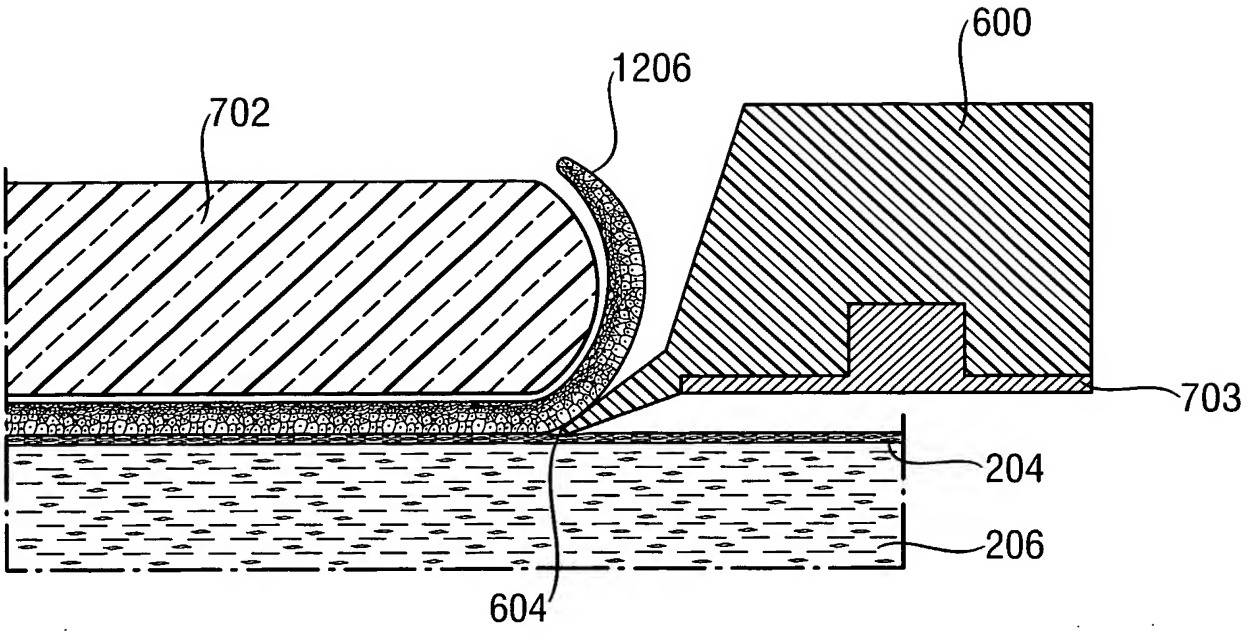


Fig. 14A

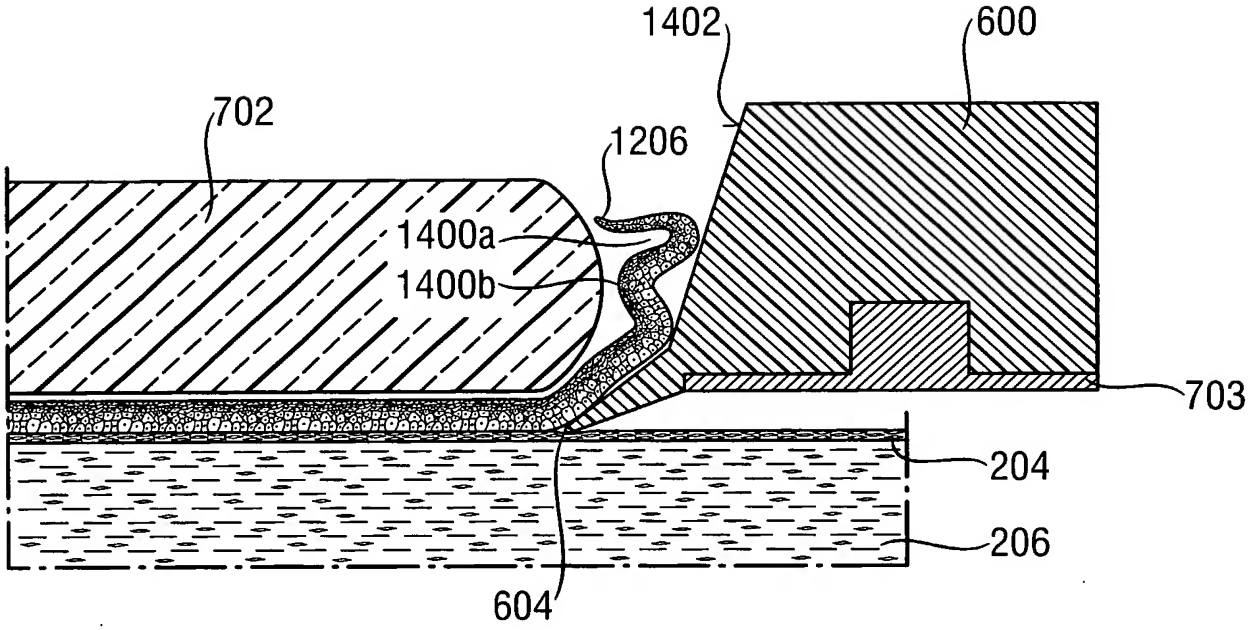


Fig. 14B

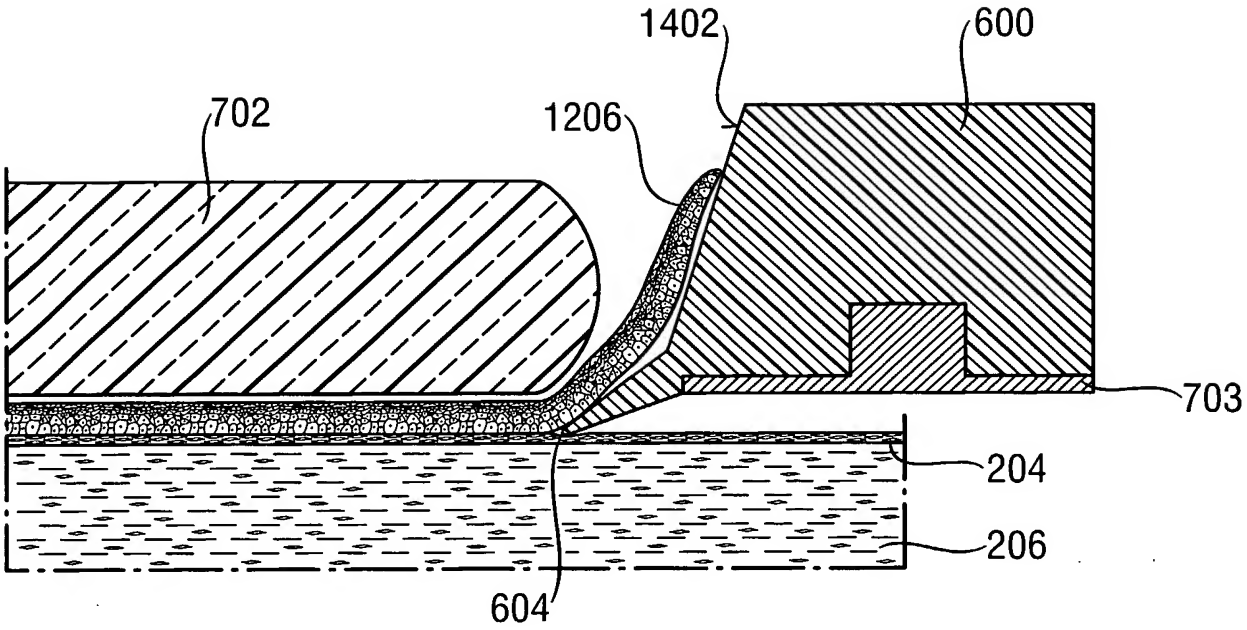


Fig. 14C

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/13955

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61F9/013

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61F A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2002/052614 A1 (GEBAUER DETLEV P) 2 May 2002 (2002-05-02) cited in the application the whole document	1,3,4, 10-12
Y	US 2002/026101 A1 (BOOKWALTER JOHN R ET AL) 28 February 2002 (2002-02-28)	3,4, 10-12, 15,16, 22,23
A	abstract paragraph '0014!	11
X	WO 01/97729 A (OASIS MEDICAL INC) 27 December 2001 (2001-12-27)	14
Y	page 5, line 19 - line 22; figures	1,15,16, 21-23

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

'A' document defining the general state of the art which is not considered to be of particular relevance

'E' earlier document but published on or after the international filing date

'L' document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

'O' document referring to an oral disclosure, use, exhibition or other means

'P' document published prior to the international filing date but later than the priority date claimed

'T' later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

'X' document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

'Y' document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

'&' document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 April 2004	29/04/2004

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Wolf, C

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/13955

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	FR 2 691 625 A (UNO PLAST AS) 3 December 1993 (1993-12-03)	21
A	abstract	9
A	WO 01/93791 A (FEINGOLD VLADIMIR) 13 December 2001 (2001-12-13) page 7, line 1 -page 8, line 17; figures 5-7	1,3,4, 10-12, 15,16

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/13955

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 26, 27
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/EP 03/13955

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2002052614 A1	02-05-2002	DE 10051215 A1	08-05-2002
		DE 20023239 U1	10-07-2003
		EP 1199055 A1	24-04-2002
US 2002026101 A1	28-02-2002	US 6241659 B1	05-06-2001
		EP 1090589 A1	11-04-2001
WO 0197729 A	27-12-2001	US 2003004526 A1	02-01-2003
		AU 6700901 A	02-01-2002
		CA 2410357 A1	27-12-2001
		EP 1294328 A1	26-03-2003
		WO 0197729 A1	27-12-2001
FR 2691625 A	03-12-1993	DK 72592 A	30-11-1993
		DE 9308046 U1	12-08-1993
		FI 1031 U1	19-11-1993
		FR 2691625 A3	03-12-1993
		IT T0930120 U1	29-11-1993
		SE 9301832 A	30-11-1993
WO 0193791 A	13-12-2001	US 6599305 B1	29-07-2003
		AU 4772301 A	17-12-2001
		EP 1289456 A1	12-03-2003
		WO 0193791 A1	13-12-2001
		WO 03015674 A1	27-02-2003
		US 2004059361 A1	25-03-2004